

In the Claims:

Claims 1-192 (Canceled).

193. (New) A method of generating cells capable of secreting insulin, the method comprising:

- (a) subjecting mammalian embryonic stem cells to a first set of culturing conditions selected suitable for differentiation of at least a portion of said mammalian embryonic stem cells into cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype; and
- (b) subjecting said cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype to a second set of culturing conditions selected suitable for formation of surface bound cell clusters including insulin producing cells, thereby generating cells capable of secreting insulin.

194. (New) A method of producing insulin, the method comprising:

- (a) subjecting mammalian embryonic stem cells to a first set of culturing conditions selected suitable for differentiation of at least a portion of said mammalian embryonic stem cells into cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype; and
- (b) subjecting said cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype to a second set of culturing conditions selected suitable for formation of surface bound cell clusters including insulin producing cells, thereby producing the insulin.

195. (New) The method of claim 193, further comprising:

- (c) isolating said surface bound cell clusters and optionally isolating said insulin producing cells therefrom.

196. (New) The method of claim 193, further comprising:
- (c) dissociating said surface bound cell clusters into single cells including said insulin producing cells; and
 - (d) subjecting said single cells to a third set of culturing conditions selected suitable for maintaining said insulin producing cells in culture for at least 14 days.
197. (New) The method of claim 196, further comprising:
- (e) isolating said insulin producing cells.
198. (New) The method of claim 196, wherein said third set of culturing conditions is selected suitable for maintaining said insulin producing cells in suspended cell clusters.
199. (New) The method of claim 198, wherein said suspended cell clusters are characterized by a proportion of said insulin producing cells of at least 4 percent.
200. (New) The method of claim 198, wherein an insulin secretion rate capacity of said insulin producing cells of said suspended cell clusters is at least 6 microunits insulin per one hundred thousand cells per hour.
201. (New) The method of claim 194, further comprising:
- (c) harvesting the insulin..
202. (New) The method of claim 198, further comprising:
- (e) isolating said suspended cell clusters.
203. (New) The method of claim 196, wherein said third set of culturing conditions is selected suitable for inhibiting growth of substantially non insulin producing cells.
204. (New) The method of claim 203, wherein said substantially non insulin producing cells are neurons and/or mesenchymal cells.

205. (New) The method of claim 196, wherein said dissociating said surface bound cell clusters into single cells is effected by trypsinization of said surface bound cell clusters.

206. (New) The method of claim 196, wherein said third set of culturing conditions includes a condition selected from the group consisting of a substantially serum free culture medium, a basic fibroblast growth factor free culture medium, a culture medium including nicotinamide, a culture medium including a synthetic serum supplement, a culture medium including glucose at a concentration of 15 millimolar or less, and inhibiting adherence of said insulin producing cells to a surface.

207. (New) The method of claim 193, wherein said first set of culturing conditions is selected suitable for inducing formation of embryoid bodies.

208. (New) The method of claim 193, wherein said first set of culturing conditions is selected capable of inhibiting adherence of said mammalian embryonic stem cells to a surface.

209. (New) The method of claim 193, wherein said at least one characteristic associated with a pancreatic islet cell progenitor phenotype is expression and optionally display of nestin.

210. (New) The method of claim 193, further comprising:

- (c) dissociating said cells displaying at least one characteristic associated with a pancreatic islet phenotype into single cells displaying at least one characteristic associated with a pancreatic islet phenotype; and
- (d) subjecting said single cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype to a fifth set of culturing conditions selected suitable for proliferation of said cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype prior to step (b).

211. (New) The method of claim 210, wherein said fourth set of culturing conditions includes a culturing condition selected from the group consisting of a

substantially serum free culture medium, a culture medium including insulin, a culture medium including transferrin, a culture medium including fibronectin, a culture medium substantially including selenium, and facilitating adherence of said cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype to a surface.

212. (New) The method of claim 193, wherein said second set of culturing conditions is selected suitable for formation of cell clusters including cells displaying at least one characteristic associated with a pancreatic islet cell phenotype selected from the group consisting of an endocrine cell precursor phenotype, an alpha cell phenotype, a beta cell phenotype, a delta cell phenotype, and a neuronal cell phenotype.

213. (New) The method of claim 193, wherein said second set of culturing conditions is selected suitable for formation of cell clusters including insulin producing cells capable of displaying a change in an insulin secretion in response to a drug selected from the group consisting of an increase in said insulin secretion wherein said drug is tolbutamide, an increase in said insulin secretion wherein said drug is IBMX, a decrease in said insulin secretion wherein said drug is diazoxide, a decrease in said insulin secretion wherein said drug is nifedipine, and a decrease in said insulin secretion wherein said drug is carbachol.

214. (New) The method of claim 193, wherein said mammalian embryonic stem cells are human embryonic stem cells.

215. (New) The method of claim 214, wherein said human embryonic stem cells are selected from the group consisting of I6 cells, H9 cell derived cells, and H13 cells.

216. (New) The method of claim 215, wherein said H9 cell derived cells are H9.2 cells.

217. (New) An insulin producing cell cluster comprising insulin producing cells being maintainable in culture for at least 14 days, wherein a proportion of said insulin producing cells in the cell cluster is at least 4 percent.

218. (New) The insulin producing cell cluster of claim 217, wherein said proportion of said insulin producing cells in the cell cluster is at least 32 percent.

219. (New) The insulin producing cell cluster of claim 217, wherein an insulin secretion rate capacity of said insulin producing cells is at least 6 microunits insulin per one hundred thousand cells per hour.

220. (New) The insulin producing cell cluster of claim 217, wherein the cell cluster further comprises cells displaying at least one characteristic associated with a pancreatic islet cell phenotype selected from the group consisting of an endocrine cell precursor phenotype, an alpha cell phenotype, a beta cell phenotype, a delta cell phenotype, and a neuronal cell phenotype

221. (New) The insulin producing cell cluster of claim 217, wherein said insulin producing cell cluster produces human insulin.

222. (New) The insulin producing cell cluster of claim 217, wherein said insulin producing cell cluster includes human cells.

223. (New) The insulin producing cell cluster of claim 222, wherein said human cells have a genotype of I6 cells, H9 cell derived cells, and H13 cells.

224. (New) The insulin producing cell cluster of claim 223, wherein said H9 cell derived cells are H9.2 cells.

225. (New) A method of treating a pancreatic disease in a subject, the method comprising:

- (a) subjecting mammalian embryonic stem cells to a first set of culturing conditions selected suitable for differentiation of at least a portion of said mammalian embryonic stem cells into cells displaying at least one

characteristic associated with a pancreatic islet cell progenitor phenotype;

- (b) subjecting said cells displaying at least one characteristic associated with a pancreatic islet cell progenitor phenotype to a second set of culturing conditions selected suitable for formation of surface bound cell clusters including insulin producing cells; and
- (c) administering a therapeutically effective dose of said insulin producing cells to the subject, thereby treating the pancreatic disease.

226. (New) The method of claim 225, further comprising isolating said surface bound cell clusters and optionally said insulin producing cells therefrom prior to step (c).

227. (New) The method of claim 225, further comprising:

- (d) dissociating said surface bound cell clusters into single cells including said insulin producing cells; and
- (e) subjecting said single cells to a third set of culturing conditions selected suitable for maintaining said insulin producing cells in culture for at least 14 days prior to step (c).

228. (New) The method of claim 225, wherein a total insulin secretion capacity of said insulin producing cells of said suspended cell clusters is at least 0.50 microunits insulin per one hundred thousand cells.

229. (New) The method of claim 225, wherein said mammalian embryonic stem cells are human embryonic stem cells.

230. (New) The method of claim 229, wherein said human embryonic stem cells are selected from the group consisting of I6 cells, H9 cell derived cells, and H13 cells.

231. (New) The method of claim 230, wherein said H9 cell derived cells are H9.2 cells.

232. (New) The method of claim 225, wherein said insulin producing cells are syngeneic with or allogeneic with the subject.

233. (New) The method of claim 225, wherein the subject is a human or a non human mammal.

234. (New) The method of claim 225, wherein said administering is effected by transplantation or injection of said insulin producing cells into the pancreas of the subject.